

PATENT
(710/202D)

Attorney Docket No. 112800.301

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Keith Henry Stockman Campbell et al.

Serial No.: 09/658,862

Filed: September 8, 2000

)
)
)
)
)
)
)

Group Art Unit: 1632

Examiner: D. Crouch

For: UNACTIVATED OOCYTES AS CYTOPLAST
RECIPIENTS FOR NUCLEAR TRANSFER**RECEIVED**

MAR 05 2003

Commissioner for Patents
Washington, DC 20231

TECH CENTER 1600/2900

Sir:

DECLARATION OF DR. DAVID WELLS UNDER 37 C.F.R. § 1.132

I, David Wells, declare that:

1. Since 1992, I have held the position of Research Scientist, AgResearch, Ruakura, New Zealand. I am a principal researcher in the field of nuclear transfer with embryonic and somatic cells and have been involved in the establishment of embryonic stem (ES) cell technology at AgResearch. In part, my research involves cloning livestock animals, particularly sheep and cattle, from cultured cells using nuclear transfer into oocytes. I have conducted many studies using nuclear transfer into oocytes and developing the resultant embryos into fetuses and animals. A copy of my Curriculum Vitae is attached hereto.

2. From 1987 to 1988, I held the position of Research Scientist, MAF Technology, Ruakura, New Zealand. During my employment with MAF Technology I

Serial No.: 09/658,862
Declaration of Dr. David Wells

developed an embryo splitting technique, which was integrated into a large scale multiple ovulation and embryo transfer program conducted at Hopu Hopu Quarantine Research Station in New Zealand. My research involved cloning sheep by embryo splitting. This involved embryo manipulation and culture and the development of identical twin animals by transfer into hosts.

3. In 1991, I graduated with a Doctor of Philosophy from the University of Edinburgh, UK. I conducted the research for my PhD thesis at the Department of Reproduction and Development, AFRC Institute of Animal Physiology and Genetics Research, Roslin Institute, and the Department of Genetics, at the University of Edinburgh. During my PhD program, I worked in Dr. Ian Wilmut's laboratory and developed competence in embryonic stem (ES) cell isolation. My work involved using isolated ES cells to generate germline chimeras by embryo manipulation and culture and the development of animals.

4. I have published numerous manuscripts in the area of cloning livestock animals from cultured cells using nuclear transfer. Two representative manuscripts are: "Production of cloned lambs from an established embryonic cell line: a comparison between in vivo- and in vitro-matured cytoplasts" published in *Biology of Reproduction* 57: 385-393 (1997) and "Production of cloned calves following nuclear transfer with cultured adult mural granulosa cells" published in *Biology of Reproduction* 60: 996-1005 (1999).

5. I have read U.S. Patent 5,057,420 of Massey, a copy of which is attached hereto.

6. Massey discusses the use of bovine embryos isolated from cows for nuclear transfer.

Serial No.: 09/658,862
Declaration of Dr. David Wells

7. Based on Massey and on my experience in cloning mammals, the embryos and bovines of Massey do not contain the same set of chromosomes as a single parental mammal. This is because the embryos and bovines of Massey were generated from bovine embryonic cells. The embryos from which these cells were derived were the product of normal sexual reproduction. Consequently, the embryos and bovines of Massey had two parents, one male and one female. The embryos and bovines of Massey had a chromosomal donation from each of these parents. Therefore, the embryos and bovines of Massey do not contain the same set of chromosomes as either of their parents.

8. Based on Massey and on my experience in cloning mammals, the embryos of Massey could be distinguished from an embryo that contains the same set of chromosomes as a single parental mammal by various techniques. Differences and identities in chromosomes could be readily determined, for example, using the well-known technique of genetic analysis.

9. I have read pages 48, 49, and 51-56 in *The Science of Providing Milk for Man* by Campbell and Marshall, copies of which are attached hereto.

10. Campbell and Marshall discuss bovines.

11. Based on Campbell and Marshall and on my experience in cloning mammals, the bovines of Campbell and Marshall do not contain the same set of chromosomes as a single parental mammal. This is because the bovines of Campbell and Marshall were the product of normal sexual reproduction. Consequently, the bovines of Campbell and Marshall had two parents, one male and one female. The bovines of Campbell and Marshall had a chromosomal donation from each of these

Serial No.: 09/658,862
Declaration of Dr. David Wells

parents. Therefore, the bovines of Campbell and Marshall do not contain the same set of chromosomes as either of their parents.

12. Based on Campbell and Marshall and on my experience in cloning mammals, the bovines of Campbell and Marshall could be distinguished from a mammal that contains the same set of chromosomes as a single parental mammal by various techniques. Differences and identities in chromosomes could be readily determined, for example, using the well-known technique of genetic analysis.

13. I have read an article by Sims et al. in *Proc. Natl. Acad. Sci.* 90, 6143-6147 (1993), a copy of which is attached hereto.

14. Sims et al. discusses the production of embryos and bovines by nuclear transfer using bovine embryonic cells as nuclear donors.

15. Based on Sims et al. and on my experience in cloning mammals, the embryos and bovines of Sims et al. do not contain the same set of chromosomes as a single parental mammal. This is because the embryos and bovines of Sims et al. were generated from bovine embryonic cells. The embryos from which these cells were derived were the product of normal sexual reproduction. Consequently, the embryos and bovines of Sims et al. had two parents, one male and one female. The embryos and bovines of Sims et al. had a chromosomal donation from each of these parents. Therefore, the embryos and bovines of Sims et al. do not contain the same set of chromosomes as either of their parents.

16. Based on Sims et al. and on my experience in cloning mammals, the embryos and bovines of Sims et al. could be distinguished from an embryo or mammal that contains the same set of chromosomes as a single parental mammal by various

Serial No.: 09/658,862
Declaration of Dr. David Wells

techniques. Differences and identities in chromosomes could be readily determined, for example, using the well-known technique of genetic analysis.

17. I have read WO 95/17500 published June 29, 1995, of Stice et al., a copy of which is attached hereto.

18. Stice et al. discusses the production of genetically modified embryos and mammals by nuclear transfer using genetically modified embryonic cells as nuclear donors.

19. Based on Stice et al. and on my experience in cloning mammals, the genetically modified embryos and mammals of Stice et al. did not receive their chromosomes from a single parental mammal. This is because the genetically modified embryos and mammals of Stice et al. were generated from genetically modified embryonic cells. The embryos from which these cells were derived were the product of normal sexual reproduction. Consequently, the genetically modified embryos and mammals of Stice et al. had two parents, one male and one female. The genetically modified embryos and mammals of Stice et al. had a chromosomal donation from each of these parents. Therefore, the genetically modified embryos and mammals of Stice et al. did not receive their chromosomes exclusively from one of their parents.

20. Based on Stice et al. and on my experience in cloning mammals, the genetically modified embryos and mammals of Stice et al. could be distinguished from an embryo or mammal that receives its chromosomes from a single parental mammal by various techniques. Differences and identities in chromosomes could be readily determined, for example, using the well-known technique of genetic analysis.

21. Based on my experience with mammals cloned by nuclear transfer and mammals propagated by sexual reproduction, the source of a mammal's chromosomes

Serial No.: 09/658,862
Declaration of Dr. David Wells

can be readily determined using genetic analysis. By using genetic analysis, whether a mammal is a cloned asexually by somatic cell nuclear transfer or propagated by sexual reproduction, including a mammal produced by nuclear transfer from an embryonic cell, can be determined by comparing the chromosomal DNA of the mammal to that of its parent(s). Only a mammal cloned by somatic cell nuclear transfer will contain the same set of chromosomes as a single parental mammal.

22. Based on my experience with mammals cloned by nuclear transfer and mammals propagated by sexual reproduction, a mammal cloned by somatic cell nuclear transfer is unlike any mammal produced by a process involving sexual reproduction, including a mammal produced by nuclear transfer from an embryonic cell. The set of chromosomes of a mammal cloned by somatic cell nuclear transfer is obtained from a single parental mammal. The set of chromosomes from any mammal produced by a process involving sexual reproduction, including a mammal produced by nuclear transfer from an embryonic cell, comes from two parental mammals, one male and one female. This feature allows the cloned mammal to preserve the genetic information of the parental mammal without dilution.

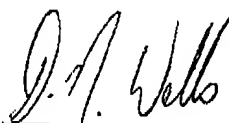
23. Based on my experience with cloned mammals, a mammal that contains the same set of chromosomes as a single parental mammal can be distinguished from the parental mammal due to environmental influences. First, the cloned mammal will always be of a younger age than the parental mammal. Second, the cloned mammal will have a variety of phenotypic differences from the parental mammal, for example, differences in fur and skin pigmentation. Third, the cloned mammal will have behavioral differences from the parental mammal.

N/A

Serial No.: 09/658,862
Declaration of Dr. David Wells

24. The undersigned further declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing therefrom.

Dated: 26th February 2003

By: 
David Wells, Ph.D